

In the Claims

1-18 (canceled).

19 (currently amended). A method for selecting or preparing cells comprising at least one metabolic pathway or metabolic pathway family enabling the transformation of at least one substrate {Ai} into a desired product {B}, comprising the following steps:

- a) providing a population of host cells (Ai- ; B-) incapable of metabolizing said at least one substrate {Ai} and said product {B};
- b) transforming said population of host cells with a library of sequences of nucleic acid;
- c) testing ~~in parallel the growth capacity the ability~~ of said population of transformed host cells to grow on a first-minimum medium containing either at least one substrate {Ai} as the only source of an element essential to growth and testing the ability of said population of transformed host cells to grow on another minimum medium containing ~~on a second minimum medium containing~~ said product {B} as the only source of an element essential to growth; and
- d) selecting said host cell(s) capable of growth on the first-minimum medium containing said at least one substrate {Ai} and on the second-minimum medium containing said product {B} so that host cell(s) having a phenotype (Ai+ ; B+) is selected, and wherein host cell(s) having the phenotype (Ai+ ; B+) comprises at least one metabolic pathway or metabolic pathway family enabling the transformation of at least one substrate {Ai} into the desired product {B}, and wherein i is a whole number between 1 and 100.

20 (previously presented). The method according to claim 19, comprising, before step c), a step consisting of testing said population of transformed host cells on a minimum medium containing the substrate(s) {Ai} and said product {B} as the only source of an element essential to growth and selecting said host cell(s) capable of growth on said minimum medium containing the

substrate(s) {Ai} and said product {B}; said selected host cell(s) then being subjected to step c) and the subsequent steps.

21 (withdrawn). The method according to claim 19, comprising, after step d), the following steps:

- e) implementing *in vitro* mutagenesis of the molecule of nucleic acid isolated from said transformed host cell(s) (Ai+ ; B+) in step d);
- f) re-transforming the population of host cells (Ai- ; B-) described in step a) with the population of nucleic acids mutated *in vitro* in step e) and testing the host cell(s) thus transformed on a minimum medium containing either one of the substrate(s) {Ai}, or said product {B} as the only source of an element essential to growth; and
- g) selecting said transformed host cell(s) incapable of growth on a minimum medium containing one of the substrate(s) {Ai} and capable of growth on a minimum medium containing said product {B} (Ai- ; B+), and optionally isolating the mutated molecule of nucleic acid.

22 (withdrawn). The method according to claim 21, comprising the characterization of the gene or genes encoding the enzyme or enzymes involved in the conversion of the substrate {Ai} into product {B} in said host cell(s) (Ai- ; B+) selected in step g).

23 (withdrawn). The method according to claim 21, comprising, after step f), in parallel to step g):

- h) selecting said transformed host cell(s) which has (have) become incapable of growth on a minimum medium containing one of the substrate {Ai} and on a minimum medium containing said product {B} (Ai- ; B-);
- i) implementing a quantitative analysis of the accumulation of the product {B} of said transformed host cells(s) (Ai- ; B-) on a rich medium supplemented by {Ai}; and

j) selecting said transformed host cell(s) (Ai- ; B-) accumulating the product {B} on a rich medium and optionally isolating in parallel the mutated molecule of nucleic acid introduced during the transformation of step f).

24 (withdrawn). The method according to claim 23, comprising the characterization of the gene or genes encoding the enzyme or enzymes involved in the conversion of the substrate {Ai} into product {B} in said host cell(s) (Ai- ; B-) selected in step j).

25 (previously presented). The method according to claim 19, comprising, after step c), in parallel to step d) and the subsequent steps, the following steps:

- k) selecting said transformed host cell(s), incapable of growth on a minimum medium containing one of the substrates {Ai} and capable of growth on a minimum medium containing said product {B}, called receiving cell(s) (Ai- ; B+);
- l) transforming said receiving cell(s) (Ai- ; B+) with a library of sequences of nucleic acid;
- m) testing in parallel said transformed receiving cell(s) (Ai- ; B+) on a minimum medium containing one of the substrates {Ai};
- n) selecting said transformed receiving cell(s) capable of growth on a minimum medium containing one of the substrates {Ai}; and
- o) characterizing the nucleic acid encoding an enzyme or enzymes involved in the conversion of the substrate {Ai} into product {B} in said transformed receiving cell(s) (Ai+ ; B+) selected in step n).

26 (previously presented). The method according to claim 25, comprising, before step m), testing said host cell(s) (Ai- ; B+) transformed on a minimum medium containing several substrates {Ai} as the only source of an element essential to growth and selecting said host cell(s) capable of growth on said minimum medium containing several substrates {Ai}; said selected host cell(s) then being subjected to step m) and the subsequent steps.

27 (withdrawn). The method according to claim 25, wherein:

- between steps k) and l), said host cell(s) (Ai- ; B+) is/are modified by replacing the first selection marker present in the vector containing the sequence of nucleic acid introduced in step b) with a new selection marker;
- said library of sequences of nucleic acid from step l) includes a selection marker different to that carried by said host cell(s) (Ai- ; B+); and
- the method further includes the following steps:
 - kk) the extraction and purification of the vectors contained in said host cell(s) selected in step k);
 - kkk) the *in vitro* mutagenesis of said vector purified in step kk), advantageously by transposition with a transposable element carrying a functional resistance to an antibiotic different to that previously existing on this vector;
 - kkkk) the transformation of said host cell(s) (Ai- ; B-) incapable of metabolising said substrate(s) {Ai} and said product {B} by the mutated nucleic acids obtained in the previous step; and
 - kkkkk) the selection of transformed host cells containing just said second selection marker; these transformed cells, of phenotype (Ai-B+), called receiving cells, are then the object of the transformation described in step l).

28 (withdrawn). The method according to claim 19, wherein said host cells are eukaryotic or prokaryotic cells.

29 (withdrawn). The method according to claim 28, wherein said host cells are:

- cultivatable under standard conditions known by the man skilled in the art,
- transformable, and
- capable of stably maintaining a transforming exogenous DNA.

30 (withdrawn). The method according to claim 28, wherein said host cells are bacteria.

31 (previously presented). The method according to claim 19, wherein said library of sequences of nucleic acid is a metagenomic library.

32 (previously presented). The method according to claim 19, in which said library of nucleic acid sequences originates from cultivatable prokaryotic or eukaryotic organisms.

33 (previously presented). The method according to claim 19, in which said library of nucleic acid sequences originates from non-cultivable prokaryotic or eukaryotic organisms.

34-35 (canceled).

36 (withdrawn). A method for selecting or preparing a host cell (Ai- ; B-) incapable of metabolising said substrate(s) {Ai} and said product {B} comprising the following steps:

- testing a population of host cells, cultivatable under standard laboratory conditions and under industrial production conditions, transformable, and capable of stably maintaining the transforming exogenous DNA, on a minimum medium containing the substrate(s) {Ai} and said product {B} as the only source of an element essential to growth; and,
- selecting the host cell(s) incapable of growth on said minimum medium containing the substrate(s) {Ai} and said product {B}.

37 (previously presented). The method according to claim 32, wherein said cultivatable prokaryotic organism is a bacterium.

38 (previously presented). The method according to claim 33, wherein said non-cultivable prokaryotic organism is a bacterium.

39 (previously presented). The method according to claim 19, wherein said library of sequences has a high GC content canceled.

40 (previously presented). The method according to claim 19, wherein said host cell is *Streptomyces lividans*.